PCRM PHYSICIANS COMMITTEE FOR RESPONSIBLE MEDICINE
5100 WISCONSIN AVENUE, N.W., SUITE 400
WASHINGTON, DC 20016
T: (202) 686-2210 F: (202) 686-2216
PCRM@PCRM.ORG WWW.PCRM.ORG

June 16, 2004

Michael O. Leavitt, Administrator
US Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

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Subject: Comments on the HPV test plan for the chemical 2,4,8,10-Tetraoxa-3,9-diphosphaspiro[5.5]undecane, 3,9-bis(octadecyloxy)-

Dear Administrator Leavitt:

The following are comments on the test plan for the chemical 2,4,8,10-Tetraoxa-3,9-diphosphaspiro[5.5]undecane, 3,9-bis(octadecyloxy)- (Weston 618, CAS # 13806-34-6) for the HPV program, submitted by the Crompton Corporation. These comments are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal, health and environmental protection organizations have a combined membership of more than ten million Americans.

Crompton proposes to do an OECD 421 screening protocol on this chemical, which will kill approximately 675 animals. It also proposes to do a hydrolysis study. We appreciate the use of modeling to fulfill aquatic toxicity data, but believe that additional animal testing is not required.

Participants are encouraged by the EPA (see *http://www.epa.gov/chemrtk/ceoltr2.htm*) to use all measures available to eliminate animal testing, including existing data, structure-activity and metabolism considerations, and *in vitro* assays. Given that some participants, in recent test plans, have used existing data on hydrolysis products of the HPV chemicals to eliminate animal tests (for an example, see Triisopropylborate, *http://www.epa.gov/chemrtk/triprobt/c14841tc.htm*), Crompton should first conduct the necessary hydrolysis study at the pH appropriate to the stomach conditions of mammals. The reproductive and developmental toxicities of the resulting products may be known, or they may have characteristics that would preclude their testing, such as a strong corrosive nature.

After the hydrolysis study has been conducted, if there is still a need for reproductive and developmental data for this chemical, Crompton should consider fulfilling the developmental endpoint using the rodent embryonic stem cell test (EST), especially since the HPV program is a screening level program. The European Centre has validated this *in vitro* embryotoxicity test method for the Validation of Alternative Methods, and the Centre's Scientific Advisory Committee has concluded that this test

is ready to be considered for regulatory purposes (Genschow 2002). The cost of the EST is a fraction of the cost of the 421 protocol. We would be happy to provide further information on a laboratory that conducts this test. Together with the histopathology data on reproductive organs from the repeat dose study in the robust summary, it is possible for Crompton to fulfil the data gaps for this chemical without conducting further animal testing.

Thank you for your attention to this issue. I look forward to a prompt and favorable response to our concerns. I can be reached at 202-686-2210 ext. 335 or via email at *kstoick@pcrm.org*.

Sincerely,

Kristie Stoick, MPH
Research Analyst

Chad B. Sandusky, PhD
Director of Research